The contemporary management of neck pain in adults

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PRACTICE POINTS

- Neck pain is an important public health problem with high levels of disability worldwide.
- The prognosis of neck pain is favourable for the first six weeks with significant reduction in pain intensity and disability.
- A large proportion of people with neck pain tend to develop chronic or persistent symptoms.
- Best evidence supports non-pharmacological interventions (eg, exercise, manual therapy and education) instead of pharmacological interventions for the management of neck pain.
- Our findings are limited by the small number of studies and poor methodological quality.

ABSTRACT

Neck pain is a common condition with a high prevalence worldwide. Neck pain is associated with significant levels of disability and is widely considered an important public health problem. Neck pain is defined as pain perceived between the superior nuchal line to the spinous process of the first thoracic vertebra. In some types of neck conditions, the pain can be referred to the head, trunk and upper limbs. This perspective article aims to provide an overview of the available evidence on prevalence, costs, diagnosis, prognosis, risk factors, prevention and management of patients with neck pain.

Epidemiology and costs

According to the Global Burden of the Disease, neck pain is ranked fourth in terms of years lived with disability globally [1]. The point prevalence of neck pain is estimated as 8% [2], the 1-month prevalence is 23%, the 1-year prevalence is 37%, and finally, the lifetime prevalence can be as high as 48% [2]. The overall prevalence of neck pain tends to be higher in women than men across all ages groups [3]. The peak prevalence of neck pain occurs between 45-49 years in males (about 9 per 100,000 inhabitants) and between 45-54 years in females (about 13 to per 100,000 inhabitants) [3]. High-income countries tend to have higher prevalence rates than low- and middle-income countries [3, 4]. One possible explanation for this would be the greater number of elderly, obese and sedentary people in high-income countries [3]. We also observed a higher prevalence of neck pain in urban areas than rural areas [4].

The prevalence of neck pain has also been found to be higher in the working population, with those employed in sedentary office-based roles at particularly higher risk than the general population [5]. Neck pain can result in activity limitations including reduced neck range of motion, sitting tolerance, sleep disturbance, reduced quality of life and is associated with work absenteeism [6-8]. It has an enormous economic impact due to health care costs, decreased productivity or absence from work, and expenses with work insurance [9, 10]. Patients with neck pain are responsible for an average of 11% of the visits to rehabilitation centres in the United States [11]. An estimate from the Netherlands demonstrated a total cost for neck pain of US$ 686 million annually (of which 23% was direct costs and 77% indirect costs). In the United States, it is estimated that between 1999 and 2008 there was an increase in annual spending on care related to low back and neck pain by around USD $ 487-950 per patient. In 2016 low back pain and neck pain had the highest health care costs between 154 conditions in the United States, with a total spending estimated of USD $ 134,5 billion, in which 57.2% was made by the private insurance, 33.7% by public insurance and 9.2% by out-of-pocket payments[12]. In addition, neck pain ranks second in the ranking of labour compensation in the USA [13].

Classification of neck pain

Neck pain can be classified based on the duration of symptoms, the pain pattern and the pain mechanism [13-15]. Similar to other musculoskeletal conditions, the duration of symptoms is classified as acute (up to 6 weeks), subacute (between 6 to 12 weeks) and chronic (greater than 12 weeks) [13]. The pattern of neck pain is classified into a single episode (i.e., without history

of pain and full recovery after the episode), recurrent (i.e., two or more episodes with full recovery between them) and persistent (i.e., without periods of full recovery) [14]. Finally, the pain mechanism is classified as specific (i.e., when it has an identifiable pathoanatomical cause of pain), neuropathic (originated by compression or lesion of the peripheral nervous system, such as cervical radicular syndrome [16]) and non-specific (or idiopathic i.e. not attributed to a tissue damage or specific pathology) [14, 15, 17, 18].

Whiplash associated disorders (WADs) is the term used to described bony or soft tissue injuries that occur due to a ´sudden acceleration-deceleration energy transfer to the neck´, most commonly the result of a motor vehicle accident, sports falls and others physical trauma [19-21]. The diagnosis of WADs essentially describes a specific mechanism of injury and currently the pathophysiology underpinning the disorder are not well understood. WADs are associated with a variety of symptoms including neck pain, headache, dizziness, visual and auditory disturbance. As a result, WADs are most commonly classified using the Quebec Task Force grading system based on the severity of presenting signs and symptoms: Grade 1: neck complaint, stiffness, or tenderness with no physical signs; Grade 2: neck complaint with musculoskeletal signs including decreased range of motion and point tenderness; Grade 3: neck complaint with neurologic signs, such as sensory deficits, decreased or absent deep tendon reflexes, muscle weakness; Grade 4: neck complaint with fracture or dislocation [22].

Further classifications used in the neck pain field include those made by the "international statistical classification of diseases and related health problems" (ICD), and the "associated international classification of functioning, disability an health (ICF) [16]. Classifications based on clinical findings are also commonly used in the neck pain field. The clinical practice guidelines from the *Neck Pain Task Force* [9] recommends the classification of neck pain in a four-degree system: i) no signs or symptoms suggestive of major structural pathologies and minor interference on daily activities; ii) no signs or symptoms suggestive of major structural pathologies with major interference in daily activities; iii) no signs or symptoms suggestive of major structural pathologies, but presence of neurological signs, such as decreased reflexes and weakness; and iv) signs or symptoms of major structural pathologies, such as possible red flags. A 2017 clinical practice guideline for physical therapists [13] suggests a slightly different classification but still into four categories: i) neck pain with mobility deficit; ii) neck pain with movement coordination dysfunction (includes whiplash-associated disorder); iii) neck pain with headache (cervicogenic headache); iv) neck pain with radiating pain (neurological signs) [13]. Both clinical practice guidelines suggest that treatment should be performed according to

these categories. However, we have not yet found randomized controlled trials that support the use of some of these classifications based on clinical findings to guide treatments in this population. In addition a 2020 systematic review showed that treatment-based classification systems was not more effective than alternative treatments [23].

Assessment and diagnosis

Diagnostic triage

Initial assessment of a person presenting with neck pain should begin with obtaining a thorough history of the presenting complaint and physical examination (including neurological examination). The clinical history would include obtaining information about the symptoms including radiation of pain or other symptoms such as weakness, dizziness, pain patterns, onset of symptoms including mechanism of injury, aggravating and easing factors and identification of red flags such as trauma.

Neck pain following trauma

A person presenting with neck pain following trauma should undergo additional assessment to ensure they have not sustained a serious cervical spine injury e.g., cervical spine fracture, dislocation or ligamentous instability which would require specific management such as surgery. The Canadian cervical spine rule is a clinical prediction rule that is designed to support clinical decision making in low risk patients (alert [Glasgow scale = 15], stable and under 65 years old) who present following blunt trauma[24]. This clinical prediction rule assess the need for imaging to rule out important neck spine injuries [25]. Computed tomography is the first choice exam of severe neck trauma in high risk patients (Glasgow $\leq$ 14) [26, 27]. In polytrauma patients, neck computed tomography is the first choice exam [28] and nuclear magnetic resonance contributes to the differential diagnosis for soft tissue injuries or neck spinal cord injury [28].

Screening for red flags

In the clinical evaluation we can also recognize red flags that may indicate the presence of serious pathologies [15] which include [9, 17]: fractures, vertebral dislocation, dissection of the vertebral artery, spinal cord injury, cervical myelopathy, infection, neoplasia and systemic diseases such as inflammatory arthropathies. The signs and symptoms frequently considered as red flags are [9, 15]: age under 20, age over 50 with concomitant vascular disease, signs of

neurological deficits, altered laboratory tests (erythrocyte sedimentation rate, level of reactive protein C, white blood cells), trauma, previous neck surgery, history of intravenous drug use, signs and symptoms of fever, neck stiffness, pain that does not improve regardless of the therapy used, nausea or vomiting, unexplained weight loss, excessive sensitivity to palpation of the vertebral body, severe tenderness in the neck.

The diagnostic accuracy in identifying serious diseases through the presence of red flags in patients with neck pain has not yet been validated [15, 29]. Some authors even suggest that serious neck conditions are rarely found to be associated with red flags [15, 30]. Therefore, it is recommended to monitor patients who present with one or more red flags in terms of changes/worsening of symptoms or presentation of new symptoms such as muscle weakness. Additional assessment may also be indicated, such as neurological examination (on neurological deficits), in the presence of fever (due to suspected infection) and trauma (due to the possibility of major structural injuries).

If neck pain (initial or progressively worsening) is not traumatic, complementary imaging tests will be indicated in some specific situations [29]: in suspected infection (due to the presence of fever associated with changes in laboratory test results), it is indicated nuclear magnetic resonance with or without contrast; in known malignancy. Nuclear magnetic resonance with or without contrast is also indicated for patients who have undergone previous surgeries, mainly in anterior cervical discectomy and fusion (due to the suspicion of pseudoarthrosis or problems with internal fixators), neck radiography and neck computed tomography without contrast are also indicated. The diagnosis of important diseases or neck spine injuries made through imaging is essential to guide medical practice.

Idiopathic neck pain

The use of imaging in people with idiopathic neck pain is rarely indicated. Many clinicians often relate the cause of neck pain with the degenerative changes in neck spine structures found in imaging studies. However, several neck changes are found in imaging studies in asymptomatic people and tend to increase with aging [31-37]. These findings include disc degeneration, disc protrusion, disc bulging, disc space narrowing, decrease in disc signal intensity, spinal cord compression, foraminal stenosis, decreased sagittal diameter and axial area of the dural tube and spinal cord. Therefore, in most cases, we should not relate these

radiological findings to neck pain [13]. It avoids a possible nocebo, in which verbal information from the health professional could generate a negative expectation in the patient [38].

Outcome measures

Currently, there is no core set outcomes recommended for the assessment of people with neck pain. Recent clinical practice guideline recommend clinicians to assess pain intensity, physical function and psychological aspects related to pain (e.g., anxiety, depression, catastrophization) [13]. Health-related quality of life, work status and interference of pain can complement the assessment of people with neck pain [39-41].

Pain intensity is commonly measured by the Numeric Pain Rating Scale (NPRS), ranging from 0 (no pain) to 10 (worst pain) points. The NPRS has moderate reliability for non-specific neck pain with an Intraclass Correlation Coefficient (ICC) of 0.67; (95% CI: 0.27 to 0.84) [42], and neuropathic neck pain (ICC: 0.58; 95% CI: 0.14 to 0.79) [43] and excellent reliability for cervicogenic headache (ICC: 0.92; 95% CI: 0.46 to 0.97) [44]. For disability, the Neck Disability Index (NDI) [45] is the most popular and recommended outcome measure. A 2019 systematic review [46] suggested that the NDI has excellent reliability for a 1-week test-retest interval (ICC: 0.92; 95% CI: 0.85 to 0.96). Other common measures include: the "hospital anxiety and depression scale" (HADS) (assess anxiety and depression) [47, 48]; the "pain catastrophizing scale" (PCS) (a self-report measure of catastrophizing in non-clinical and clinical population) [49]; the Tampa scale of kinesiophobia (measure the fear of movement related to pain) [50]; the short form 12 health survey [51] and EQ-5D-3L (measure quality of life) [52]; and brief pain inventory (BPI) (measure intensity of pain) [53].

Risk Factors

General Risk factors for a first episode of neck pain

A 2018 systematic review synthesized the information on the risk factors related to the development of an episode of neck pain [54]. This systematic review included 10 longitudinal studies (n = 19,055 participants) and classified the risk factors according to the strength of the association, with little association (relative risk or odds ratio between 1.0 to 1.5), moderate association (relative risk or odds ratio between 1.5 to 2.0) and high association (relative risk or odds ratio greater than 2.0) [54, 55]. The level of association between individual, physical and psychological risk factors varied from moderate to high association [54]. The authors observed

that high body mass index (> 30 kg/m^2) (OR: 2.21; 95% CI: 1.32 to 3.70), having history of neck pain (OR: 2.24; 95% CI: 1.39 to 3.06) and high perception of muscle tension (relative risk (RR): 4.04; 95% CI: 1.99 to 8.17) were risk factors with a high association for a neck pain episode. Further, risk factors such family size (composed of three people (RR: 1.50; 95% CI: 1.10 to 2.10), being male with low income (OR: 1.8; 95% CI: 1.10 to 2.70) and high perceived economic stress with low income (OR: 2.00; 95% CI: 1.30 to 3.20) were moderate risk factors. On the other hand, the authors also observed that leadership profile (OR: 0.32; 95% CI: 0.16 to 0.67), pleasant social environment (OR: 0.45; 95% CI: 0.25 to 0.83), leisure physical activity (OR: 0.6; 95% CI: 0.4 to 0.9) and good resistance of the extensor muscles (OR: 0.92; 95% CI: 0.87 to 0.97) were all protective factors. The authors conclude that most of the factors analysed are considered modifiable, and this result could possible contribute to a potential social impact. A 2019 systematic review (8 studies n = 3,345) [56] observed that people who have suffered acute neck injury due to vehicular accident, have an increased risk of developing neck pain (RR: 2.3; 95% CI: 1.8 to 3.1). Table 1 present a summary of the available evidence on the risk factors for neck pain.

Furthermore, there are increasing interest to identify risk factors for neck pain in young adults. A 2020 systematic review investigated the risk factors for non-specific neck pain in young adults [57]. This systematic review included 6 studies (n = 8,856 participants) identifying a total of 56 risk factors in young adults on 18-29 years of age. The authors observed that 56 risk factors assessed were covered on all ICF components such as, 24 risk factors (body functions and structures), 15 risk factors (activities and participation), 10 risk factors (environmental), 10 risk factors (personal factors), and female sex, BMI, perceived stress, duration of daily computer and physical activity were risk factors assessed in more than one study. There is very low to low quality of evidence that perceived stress (OR: 1.7; 95% CI: 1.1 to 2.6), utilizing a computer for at least two 4 hour with no break (OR: 1.8; 95% CI: 1.2 to 2.9), computer screen not adjusted at eye level (OR: 1.6; 95% CI: 1.1 to 2.4), keyboard positioned too high (OR: 2.2; 95% CI: 1.2 to 3.9) and 2nd year students (versus 1st year) (OR: 1.9; 95% CI: 1.1 to 3.4) are associated with developing a first episode of neck pain. Female gender demonstrated inconsistent results between three studies, and high body mass index, physical activity level, utilizing computer for neither less nor more than 3 hour per day are not associated with developing a first episode of neck pain. The authors emphasize the number of studies assessing potential risk factors with spurious findings are worrying, and the need for more high-quality studies.

Prognosis

There is a lack of high-quality prognostic studies in patients with neck pain [58, 59]. The latest systematic review summarized the evidence related to the prognosis of patients with acute non-specific neck pain [58]. This review included three cohort studies and three randomized controlled trials (pooled n = 283 participants) [58]. The authors observed a significant reduction in pain intensity and disability in the first six weeks after the onset of symptoms. The mean reduction in pain intensity in the first six weeks was 35 points (95% CI: 32 to 38) and the mean reduction in disability in the six weeks was 17 points (95% CI: 15 to 19), both measured on 0-100 scales. From six to 52 weeks, pain intensity tends to increase and those patients who did not recover are more likely to develop chronic neck pain [58]. In addition, data from an inception cohort study show that about half of the patients will fully recover up to 12 months [60]. Residual symptoms and recurrences between one to five years of initial episode are seen in 50% to 85% of patients, respectively [15, 61, 62]. The current evidence on prognosis shows that patients with neck pain have a favourable initial clinical course, but there is a significant burden on patients over time [58-60].

Prognostic factors

Several studies have investigated prognostic factors and their influence on the clinical course of patients with neck pain [60, 63-65]. A systematic review with six prospective longitudinal studies, (pooled n= 2,446 participants) investigated the prognostic factors for persistent non-specific neck pain after a first episode [66]. The authors summarised the overall quality of evidence for pain intensity and perceived non-recovery at three, six and 12 months [66]. The authors found very low to low quality of evidence that male gender (OR: 3.1; 95% CI: 1.5 to 6.7), presence of kinesiophobia (OR: 1.09; 95% CI: 1.02 to 1.15), co-existing low back pain (OR: 1.6; 95% CI: 1.1 to 2.2) and age between 45 and 59 years (OR: 3.9; 95% CI: 2.2 to 6.7) are associated with a worse prognosis in terms of pain intensity. Low quality of evidence was found for prognostic factors associated with non-recovery; these were previous neck pain (OR: 1.67; 95% CI: 1.25 to 2.24), co-existing low back pain (OR: 2.29; 95% CI: 1.27 to 4.12) and neck pain accompanied by headache (OR: 3.33; 95% CI: 1.35 to 8.33) [66]. Table 2 presents a synthesis of the evidence on prognostic factors in non-specific neck pain. Verwoerd et al. [66] identified a number of key limitations in the available literature that impact on our current understanding of the prognosis and prognostic factors associated with persistent neck pain. These include variability in the definition of neck pain, poor description of prognostic factors

and poor methodological quality of the included studies [66]. Thus, more high-quality studies using standardised definitions are needed to better understand the prognostic factors for neck pain in the population.

Interventions to prevent neck pain

Relatively few studies have investigated the effectiveness of prevention strategies for non-specific neck pain and these present conflicting findings [67-70]. The most recent systematic review (five studies, n = 3,852) summarized the evidence related to the effectiveness of interventions that aim to prevent a new episode of neck pain [71]. The authors found two main approaches were used to prevent a new episode of neck pain; ergonomic programs (e.g., adjustment of workstation) and exercise programs (e.g., usual aerobic exercise). Very low-quality evidence suggested that there is no difference between an ergonomic program compared to minimal or no intervention in prevent new neck pain episodes (OR: 1.00; 95% CI: 0.74 to 1.35, n= 3 trials). However, there is moderate quality evidence that an exercise program is better than no intervention control in reducing the risk of a new episode of neck pain (OR: 0.32; 95% CI: 0.12 to 0.86, n= 2 trials). The authors conclude that these findings are based upon a low number of trials, most of which were conducted office workers, so additional high-quality trials are needed to strengthen these estimates. Since this systematic review was published, a recent randomized controlled trial [72] investigated a multifaceted intervention (i.e., participatory ergonomics to tailed case management program) for the prevention of musculoskeletal pain in nursing staff. The authors found that multifaceted intervention was effective compared to care as usual to reduce the risk of self-perceived of neck, shoulder and upper back pain in nursing staff (OR: 0.37; 95% CI: 0.14 to 0.96). Further, Sitthipornvorakul et al [70] investigated the effects of a walking intervention compared to no intervention in reducing the risk of a new episode of neck pain in office workers in a period of 6 months. These authors observed a positive effect of walking intervention (OR: 0.22; 95% CI: 0.06 to 0.75). Further studies are needed to investigate prevention of neck pain episodes. This evidence will allow prioritising the allocation of resources to prevention programs with known effectiveness which may have a substantial impact on reducing treatment costs and improving the quality of life and productivity of people for whom the program worked.

Treatments

The goal of treatment for people with neck pain is to reduce pain intensity and disability over time. Clinical practice guidelines use different classification systems to guide management of patients with neck pain [13, 73, 74]. The most known are risk stratification based systems that classify patients based on their risk of persistent pain (e.g. low, medium and high risk) [13, 73]. Regardless the approach used, guidelines recommend advice or education for most patients who are considered to be at low risk of chronicity in the acute phase[13, 73, 74]. This recommendation is in line with the expected course of improvement of pain and activities, and it would be expected that these patients do not require additional treatments [73]. Patients with medium or high risk for chronicity could benefit from more complex treatments combined with low-level pharmaceuticals [13, 73]. Generally, this management treatments includes non-pharmacological interventions (e.g., education, exercise, manual therapy, physical agents or multimodal approach), with the addition of pharmacological interventions as required (e.g., non-steroidal anti-inflammatory drugs) [13, 73]. Thus, as first line all guidelines focus primarily on non-pharmacological interventions neck pain patients (exception to know disease) [13, 73, 74].

Pharmacological interventions: Evidence acute/subacute/chronic

Guidelines recommend the use of pharmacological interventions for refractory presentations, be used over a short period and as an adjunct to other non-pharmacological treatments. Judicious use of non-opioid based analgesics (e.g. nonsteroidal anti-inflammatory drugs) should be considered as first line therapy. [75-81]. These recommendations are based on limited evidence and with consideration of the harms associated with opioid based analgesics.

Current evidence for pharmacological interventions is as follows. There is moderate evidence that intravenous methylprednisolone is effective in reducing pain intensity compared to placebo for patients with acute whiplash at one week [82]. There is moderate quality of evidence that nonsteroidal anti-inflammatory drugs (NSAIDs) are effective in reducing pain intensity compared to placebo for patients with neck pain at immediate term [83]. There is also moderate evidence that intramuscular lidocaine and neck stretching are effective for reducing pain compared to neck stretches alone for chronic neck pain at three months [82]. On the other hand, there are high quality of evidence that botulinum toxin type A have similar effects for reducing pain intensity compared to placebo for chronic neck pain at short term [84]. The majority of the studies in the area were designed to assess the effects of non-pharmacological treatments in neck pain patients.

Non-pharmacological treatments: Evidence acute/aubacute/chronic

With regards to physical therapy-based interventions, there is moderate quality evidence that manipulation alone is effective for reducing pain intensity and function compared to oral medication (e.g., NSAIDs and opioids) for acute/subacute neck pain at short term [78]. There is low quality evidence that exercises (stretching and strengthening) are effective for reducing pain than waiting list for patient acute radiculopathy patients at short term [77]. Further, there is low quality evidence that motor control exercises have similar effects for reduction pain intensity compared to other interventions for patients with chronic neck pain [85]. Thus, there is moderate quality evidence that exercises (stabilization and strengthening) are effective for reducing pain and improving function than waiting lists controls for patients with chronic neck pain [77]. Passive therapies, such as electrotherapy (EMS and TENS) had very low evidence of no difference from placebo interventions [79].

Psychological treatments: Evidence Acute/Subacute/chronic

With regards to psychological interventions, there is low quality evidence that psychological therapies (e.g., cognitive behavioural treatment) are effective for reducing pain intensity than other interventions in subacute neck pain [80]. Further, there is low quality evidence that psychological therapies are effective for reducing pain intensity and improving function when compared to other interventions or no treatment controls in subacute and chronic neck pain [80]. There is low quality evidence that self-management strategies have similar effects for improving function than advice on stretching [76].

Education: Evidence acute/subacute/chronic

With regards to patient education (advice), there is moderate quality evidence that patient education (educational video advice) is effective for reducing pain intensity than no treatment in acute whiplash patient at short term [76]. On the other hand, there is very low quality evidence that patient education (self-care strategies) have similar effect than no treatment in acute to chronic mechanical pain patient at short term [76].

Table 3 presents a summary of the available evidence for treating neck pain. At the moment, healthcare professionals should use the available evidence to assist in the decision-making process [86-88]. A multimodal approach should be interesting for patients with neck pain considering systematic reviews and guidelines to different neck pain disorders.

Future perspective

Our current understanding of the causes, prognosis, prevention and treatment of neck pain is limited by the relatively small number of studies and their poor methodological quality. There is particular need for research to better elucidate the pain mechanisms involved in the development of non-specific neck pain, research on the effectiveness of interventions designed to prevent and treat neck pain, and research to enable the early identification of those at risk of poor prognosis or non-recovery. In 2019, an international Delphi study was conducted to identify The New Agenda for Neck Pain Research. This resulted in the identification of 5 priority areas for neck pain research, specifically: 1) to establish the effectiveness and cost-effectiveness of available treatments, 2) translate research evidence into clinical settings, 3) identify the effectiveness of education and self-care in prevention and treatment, 4) identify causal factors for the development of neck pain, and 5) define the natural course and prognostic factors for people with neck pain [89]. Researchers and funding agencies can use this new agenda to direct research efforts towards answering the most important questions identified in the field of neck pain. In the absence of robust evidence, this leaves clinicians to use indirect or empirical evidence to guide their clinical decisions.

Table 1. Risk factors for an episode of neck pain

Risk factors	Estimate (95% CI)
BMI (> 30 kg/m^2) [54]	OR 2.21 (1.32 to 3.70)
High perceived economic stress (low income) [54]	OR 2.00 (1.30 to 3.20)
Marital status (widowed) [54]	RR 1.80 (1.10 to 2.80)
Male (low income) [54]	OR 1.8 (1.10 to 2.70)
Family size (four people) [54]	RR 1.70 (1.20 to 2.40)
Family size (three people) [54]	RR 1.50 (1.10 to 2.10)
Work at computer (for at least two 4 hour with no break) [57]	OR 1.8 (1.16 to 2.89)
Computer screen (not adjusted at eye level) [57]	OR 1.64 (1.13 to 2.36)
Keyboard position close to the body [90]	RR 1.46 (1.07 to 1.99)
Keyboard position (high) [57]	OR 2.18 (1.21 to 3.91
Adjust sitting position [54]	OR 1.80 (1.16 to 2.81)
Awkward positions [54]	OR 1.65 (1.04 to 2.60)
Sustained working positions [54]	OR 1.61 (1.05 to 2.46)
Low work task variation [90]	RR 1.27 (1.08 to 1.50)
Catastrophising [91]	WMD 6.6 (3.1 to 10.1)
Muscular tension (high perception) [54]	OR 4.04 (1.99 to 8.17)
Coworker support [54]	RR 2.43 (1.11 to 5.29)
History of neck pain [54]	OR 2.24 (1.39 to 3.06)
High perception demands (work) [54]	RR 2.14 (1.28 to 3.58)
Stress [91]	OR 2.00 (1.50 to 2.70)
Lower back pain [54]	RR 2.00 (1.60 to 2.40)
High role conflict [54]	OR 2.61 (1.09 to 6.21)
2nd year students (vs 1st year) [57]	OR 1.90(1.08 to 3.35)
Employment status (ill/disabled) [54]	RR 1.90 (1.20 to 2.90)
Fair general health (status) [54]	RR 1.80 (1.30 to 2.60)
Muscular tension (medium perception) [54]	OR 1.79 (1.03 to 3.27)
Effort-reward imbalance [54]	HR 1.66 (1.16 to 2.38)†
Sleep (poor quality/< sleep hours) [91]	OR 1.63 (1.23 to 2.18)
Poor general health (status) [54]	OR 1.62 (1.07 to 2.44)
Employment status (Part-time) [54]	RR 1.60 (1.20 to 2.20)

Anxiety [91]	OR 1.43 (1.20 to 1.70)
Prior neck injury (vehicular accident) [56]	OR 2.3 (1.8 to 3.1)
Good resistance of the extensor muscles [54]	OR 0.92 (0.87 to 0.97)
Leisure physical activity [54]	OR 0.6 (0.4 to 0.9)
Pleasant social environment [54]	OR 0.45 (0.25 to 0.83)
Low satisfaction with workplace environment[90]	RR 1.28 (1.07 to 1.55)
Leadership profile [54]	OR 0.32 (0.16 to 0.67)

BMI = Body mass index; RR= Risk ratios; HR: Hazard ratios; WMD = Weighted mean difference. Synthesis of evidence on risk factors in neck pain based on recent studies [54, 56, 91].

Table 2. Prognostic factors for patients with neck pain

Pain intensity	Odds ratio (95% CI)	Quality of evidence
Pain intensity – 3 months		
Gender (male)	3.13 (1.5 to 6.67)	Very low
Severity of complaints (less)	0.74 (0.57 to 0.95)	Very low
Kinesiophobia (TSK)	1.09 (1.02 to 1.15)	Very low
Pain intensity – 12 months		
Age (45-59 years)	3.9 (2.2 to 6.7)	Low
Not working	1.6 (1.1 to 2.3)	Very low
Cycling (regular activity)	2.4 (1.5 to 4.0)	Very low
Pain intensity at baseline	0.26 (0.07 to 0.45)$^{(\beta)}$	Very low
Low back pain	1.6 (1.1 to 2.2)	Very low
Neck pain (> 13 weeks)	1.35 (0.34 to 1.93)$^{(\beta)}$	Very low
Previous episodes of neck pain	1.35 (0.13 to 1.58)$^{(\beta)}$	Very low
Patient perceived non recovery		
Patient perceived non recovery – 3 months		
Headache	3.70 (1.47 to 9.09)	Low
Depression	1.30 (1.02 to 1.64)	-
Patient perceived non recovery – 6 months		
Age (in years)	1.03 (1.01 to 1.05)	Very low
Low back pain	2.29 (1.27 to 4.12)	Low
Previous episodes of neck pain	1.67 (1.25 to 2.24)	Low
Patient perceived non recovery – 12 months		
Gender (female)	4.55 (1.39 to 14.29)	Very low
Age (> 40 years)	3.85 (1.64 to 9.09)	Low
Low back pain	2.7 (1.25 to 5.88)	Very low

BMI = Body mass index; BQ = The Bournemouth questionnaire; TSK = Tampa scale of Kinesiophobia, 4DSQ = Four dimensions psychological symptomatology questionnaire, β = Regression coefficient 95% CI; Confidence interval estimate direction (< better and > poor prognosis). Synthesis of evidence on prognostic factors in non-specific neck pain conducted by Verwoerd [66]

Table 3. Overview of the effects of interventions for neck pain on the outcome for short-term pain intensity.

	Nº participants (studies)	**Effect estimates (95% CI)**	**Effect size**	**Quality of evidence**
Effects of interventions for acute and subacute neck pain				
Pharmacological				
Intravenous intravenous methylprednisolone (vs placebo) [82]*	39 (1 trial)	**SMD -0.90 (-1.57 to -0.24)**	Large	-
Nonpharmacological				
Manipulation alone of cervical region (vs oral medication) [78]	182 (1 trial)	**SMD -0.34 (-0.64 to -0.05)**	-	Moderate
Manipulation alone of thoracic region (vs inactive control) [78]	242 (2 trials)	SMD -1.46 (2.20 to -0.71)	-	Moderate
Patient education (educational video) (vs no treatment)* [76]	376 (1 trial)	**SMD -0.67 (-0.87 to -0.46)**	-	Moderate
Patient education (self-care strategies) (vs no treatment) [76]	44 (1 trial)	SMD 0.09 (-0.50 to 0.68)	-	Very low
Cognitive-behavioural therapy (vs other interventions) [80]	265 (3 trials)	**SMD -0.24 (-0.48 to 0.00)**	-	Low quality
Low-level laser therapy (vs placebo) [92]	116 (2 trials)	**RR 1.69 (1.22 to 2.33)**	-	-
Exercise (Stretching and strengthening) (vs waiting list) [77]	133 (1 trial)	**SMD -0.47 (-0.81 to -0.12)**	-	Low

Physiotherapy Intervention plus Extrinsic Feedback (vs physiotherapy) [93]	80 (2 trials)	**SMD -1.09 (-1.56 to -0.61)**	-	-
Active intervention (kinaesthetic and co-ordination exercises plus regular exercises) (vs regular exercises)* [94]	66 (1 trial)	WMD 0.40 (-0.79 to 1.59)	-	-
Effects of interventions for subacute and chronic neck pain				
Pharmacological				
NSAIDs (vs placebo) [83]	225 (2 trials)	**MD -16.3 (-20.6 to -12)**		Moderate
Relaxation (vs minimal intervention) [95]	393 (1 trial)	MD 20 (-40 to 80)	-	-
Epidural injections (methylprednisolone and lidocaine) (vs intramuscular methyl prednisolone and lidocaine) [82]	50 (1 trial)	**SMD -1.46 (-2.16 to -0.76)**	Large	-
Intramuscular injection	3 trials		-	-
Intramuscular lidocaine and neck stretching (vs neck stretching) [82]	1 trial	**SMD -1.36 (-1.93 to -0.80)**	Large	-
BoNT – A (vs placebo) [84]	252 (5 trials)	SMD -0.07 (-0.36 to 0.21)		High
Nonpharmacological				
Massage (vs sham laser) [81]	106 (1 trial)	SMD -0.01 (-0.38 to 0.36)	-	Very low
Manipulation and mobilization (vs inactive control) [78]	111 (1 trial)	**SMD -0.64 (-1.04 to -0.25)**	Medium	Low

Patient education (vs no treatment) [76]	46 (1 trial)	SMD 0.09 (-0.49 to 0.67)	-	Very low
Cognitive-behavioural therapy (vs no treatment) [80]	99 (3 trials)	**SMD -0.58 (-1.01 to -0.16)**	Medium	Low
Acupuncture (vs medication) [96]	30 (1 trial)	SMD 0.23 (-95 to 0.48)		Moderate
Dry needling (vs other interventions) [97]	107 (2 trials)	SMD 0.01 (-0.41 to 0.40)		-
Electrotherapy – Magnetic necklaces (vs placebo) [79]	52 (1 trial)	SMD 0.27 (-0.27 to 0.82)		Low
Electrotherapy - EMS (vs placebo) [79]	40 (1 trial)	SMD -0.36 (-0.99 to 0.27)		Very low
Transcutaneous electrical nerve stimulation (TENS) (vs sham) [98]	38 (1 trial)	MD -1 (-9.7 to 7.7)		Very low
Mechanical traction (vs placebo) [75]	84 (1 trial)	SMD -0.16 (-0.59 to 0.27)		Low
Motor control (vs other interventions) [85]	96 (2 trials)	SMD -0.33 (-0.73 to 0.08)		Low
Exercises (vs waiting list) [77]	147 (2 trials)	**MD -14.90 (-22.40 to -7.39)**	Medium	Moderate

Information extracted preferably from Cochrane reviews for the outcome pain intensity (0-100 points) at short-term follow-up (equal to or less than three months). Effect estimates on pain scale from 0 to 10 points were converted to 100-point scales. Results in bold represents significant differences between groups. Evaluation of the quality of the evidence was carried out using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) (with level of evidence from very low to high) if available by the author review.

SMD: Standardised Mean Difference; **MD**: Mean Difference; **WMD:** Weight Mean Difference; **NSAIDs**: Nonsteroidal anti-inflammatory drugs; **BoNT-A**: Botulinum toxin type A; **EMS**: Electric muscle stimulation. * Whiplash patients

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